control group of 6 patients with CAD having 2 sequential EMVM performed without any intervention was compared in a similar fashion. Data were compared utilizing a paired T-test.

Results: Unipolar voltage values in the injected area at baseline and at 4 months (10.2 mV and 9.9 mV) were similar (p=0.32). There was a significant difference (p=0.004) when comparing unipolar voltage values in the peri-injection area at baseline and follow-up (8.12mV and 9.86mV). There was no significant increase in voltage in the area surrounding the injection sites. These findings may represent an expansion in myocardial viability as reflected by an increase in unipolar voltage detected by EMVM and may have important therapeutic implications.

11:15 a.m.

814-2

Time Course of Improvement Following Stem Cell Injections in Humans With Heart Failure

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Introduction: Preliminary evidence of perfusion and functional improvement following Autologous Bone Marrow Mononuclear Cells (ABMMNC) transplantation into areas of hibernating myocardium in end-stage ischemic heart disease patients has been reported. There is no data regarding the time course of improvement. We evaluated functional and wall motion parameters in pts receiving ABMMNC up to 10 weeks.

Methods: In 14 pts with CAD and HF ABMMNC were injected into areas of hibernating myocardium utilizing electromechanical mapping (MyoStar, Cordis, USA). Baseline and weekly assessments of NYHA, CCSA and EF by 2D echocardiogram (Simpson) were performed. SPEC/TM was performed at baseline and 8 weeks after ABMMNC transplantation. ANOVA was utilized for comparisons between baseline and 8 weeks and a generalized linear model with time strata for evaluation of peak improvement over time in regard to functional class and ejection fraction.

Results: Pts had a significant reduction in total reversibility defect (from 15.15%±14.99% to 4.53%±10.61%, p=0.0202) at 8 weeks. The NYHA class and CCSA improved from baseline to 8 weeks (2.21±0.89 to 1.14±0.36, p=0.0003 and 2.64±0.84 to 1.28±0.61, p=0.0001 respectively). The EF improved from 30.5%±7.8% to 35.7%±7.8% at 8 weeks (p=0.02). The significant improvement in NYHA occurred at the 4th wk time point (p=0.000002) and for CCSA at the 7th wk time point (p=0.000006). A significant improvement in EF was also observed between the 6th and 8th wks (p=0.04).

Conclusion: These preliminary data suggest that symptomatic, functional and myocardial perfusion improvements with ABMMNC transplantation occur during the second month of follow-up. This may help to contribute to the understanding of mechanisms of improvement involved in ABMMNC transplantation.

11:30 a.m.

814-3

Autotransplantation of Bone Marrow Into Scarred Myocardium for the Improvement of Cardiac Function in Humans: Is It Durable and Safe?

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Background: We have previously shown that autotransplantation of bone marrow into scarred hibernating myocardium in man is safe and improves cardiac function in the short term (first 10 months after surgery). To investigate the durability and safety of this procedure, 14 patients with previous myocardial infarctions who received unmanipulated bone marrow injections into infarcted areas (250k injections of bone marrow diluted in autologous serum at a ratio of 1:2 and injected 1cm apart into the mid-thickness of the left ventricular infarct zone) at a time of elective bypass graft surgery, were followed-up 2 years after the operation.

Methods: Digital Dobutamine stress echocardiography was used to assess the systolic function of the left ventricle (global), coronary regions (regional) and infarct zones (segmental). Off-line analysis with 2-4 loop side-by-side comparisons, to a resolution of 16 segments and 4 wall motion grades, was required to minimise spatial, interstage and interstudy error. The wall motion score index (WMSI) was calculated by dividing the sum of all grades by the number of segments scored. Results: There were no deaths or clinically relevant arrhythmias during the 2 year follow-up. The improvement in angina class (from 3.0±0.2 to 4.8±0.2; P=0.05) and dyspnoea status (from 2.1±0.2 to 1.2±0.1; P=0.05) at 10 months after the operation was maintained after 24 months (3.3±0.2 to 1.3±0.2, respectively; P=0.05 vs prior surgery). None of the patients were re-operated or had angina that was not post-operative and had angina that was not post-operative but was admitted to hospital twice because of chest pain and another had a minor cerebrovascular accident. Echocardiography demonstrated that the peak dose improvement in segmental WMSI of areas which had both bone marrow injections and revascularisation, previously observed at 10 months (from 3.20±0.15 to 2.20±0.09; P=0.05), was maintained after 2 years (2.40±0.44; P=0.05 vs pre-surgery). Segmental WMSI of areas that were grafted alone, or injected alone, showed no improvement at any stage of the follow-up.

Conclusions: Autotransplantation of bone marrow is free of cardiac complications and the early stress induced improvement in cardiac function is durable up to a period of at least 2 years.

814-4

Mobilization of Bone Marrow Cells (Stem Cells) by Granulocyte-Colony Stimulating Factor Associated or Not With Intracoronary Stem Infusion Improves Exercise Capacity and Quality of Life in Severe Heart Failure

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Background: myocardium regeneration is emerging as a new option in the treatment of congestive heart failure (CHF). Bone marrow stromal cells (BMSC) are pluripotent and when implanted into myocardial can undergo myocardial differentiation. We hypothesized that the BMSC mobilization to peripheral circulation by granulocyte-colony stimulating factor (G-CSF) associated or not with intracoronary BMSC infusion could improve patients (pts) with severe CHF.

Methods: We prospectively studied 9 pts, mean age 50±18 years, with refractory CHF, under maximal tolerated optimized treatment with indication of heart transplantation. We compared the BMSC mobilization in CHF with a control group of pts with orthopedic disease. CHF pts were divided in two groups: (1) 3 pts with suitable peripheral venous access for apheresis procedure who underwent BMSC mobilization, collection of mononuclear cells (MNC) followed by MNC intracoronary infusion; and (2) 6 pts without venous access who underwent only BMSC mobilization. BMSC are mobilized by 600 mg GCS-F per day during at least 5 days until peripheral blood CD 34+ cells achieve > 6/mm3 by flow cytometric analysis, monthly during 4 months. Results: The peak CD34+ cells per mm3 was lower in CHF pts versus non-CHF pts (22±13 x 39±29, p=0.04). The BMSC mobilization improved (pre-before, after→>1 month follow-up): the functional class (from IV-3 to III-5 to III-1.5), I-3pts, the LVEF (MUGA) (from 21±7.7 to 27±8.6, p=0.03), the peak oxygen consumption (ml/kg/min) (from 9.6±8.1 to 11±4.1±1, p=0.01), the quality of life evaluated by the Minnesota Living with Heart Failure Questionnaire (from 70±15 to 33±13, p=0.05). The LV end diastolic diameter, the right ventricular EF, and the ejectional slope VE/Vco2 unchanged. In the 192±114 days follow-up 3 pts died from: sudden death(1), pulmonary embolism (1), and progressive CHF (1); three pts were re-treated from heart transplantation waiting list. Conclusion: The mobilization of BMSC followed by MNC intracoronary infusion is feasible in severe CHF. The mobilization of BMSC by GCS-F is impaired in CHF. The mobilization of BMSC can improve selected severe CHF pts. The mobilization of BMSC has potential to become a new hope in CHF.

Noon